



Atty. Docket No.: 3124-Z

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Richard J. Feldmann

Serial No. 09/866,925

Group Art Unit 1645

Filed: May 30, 2001

Examiner John S. Brusca

For: ALGORITHMIC DETERMINATION OF FLANKING DNA SEQUENCES
THAT CONTROL THE EXPRESSION OF SETS OF GENES IN
PROKARYOTIC, ARCHEA AND EUKARYOTIC GENOMES

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DECLARATION UNDER 37 C.F.R. 1.132

Hon. Commissioner of Patents & Trademarks
Washington, D. C. 20231

Sir:

I, Richard W. Pastor, whose address is Laboratory of Biophysics, Center for Biologics Evaluation and Research, US Food and Drug Administration, 1401 Rockville Pike, Rockville MD, 20852-1448, declare as follows:

1. I received a Ph.D. degree in Biophysics from Harvard University. I also hold a MS degree in Chemistry from Syracuse University. My work experience includes 19 years (since Ph.D.) of research related to the computer simulation of biological systems, as well as supervision of related activities. I currently serve as Chief of the Laboratory of Biophysics in at the Center for Biologics Evaluation and Research, US Food and Drug Administration.

2. I have read the patent specification for application Serial No. 09/866,925 as filed in the United States Patent &

Trademark Office on May 30, 2001 for "ALGORITHMIC DETERMINATION OF FLANKING DNA SEQUENCES THAT CONTROL THE EXPRESSION OF SETS OF GENES IN PROKARYOTIC, ARCHEA AND EUKARYOTIC GENOMES." I read the amended claims submitted October 30, 2002, [and I have read the amended claims submitted with the amendment accompanying this Declaration].

I have read the official communication from the U.S. Patent & Trademark Office dated January 8, 2003. I have considered all of the claims.

3. I wish first to direct my comments to claims 20 - 27 which, I have been advised, are the broadest claims in the application. I have been also advised that claims 28 - 37 are all dependent from claim 20 and hence I am advised include the limitations of claim 20.

Claims 20 - 27 are as follows:

20. A method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising detecting, by computer, one or more pairs of non-adjacent DNA sequences to which are bound one RNA molecule comprising of two RNA sequences.

21. A method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising detecting, by computer, changes in connectron behavior in the genome as a function of changes in the sequence of the genome.

22. A method of modifying, by computer, the expression of different gene collections in a genome, comprising detecting changes in connectron behavior that results in changes in the level of connectron control sequences caused by an exogenous stimulus.

23. A method of detecting, by computer, where and when new genes have been integrated into a host genome comprising detecting the operable link between the newly introduced gene and the existing connectron behavior in said host genome.

24. A method of detecting, by computer, the expression effect of different gene collections in a given host genome, comprising detecting the transacting behavior of connectrons between the chromosomes thereof.

25. A method of modifying a given genome comprising modifying, by computer, the connectron organization therein.

26. A method of detecting, by computer, connectron control and target sequences in a given genome comprising:

5 determining the base composition of said genome,
 determining one or more sites of control sequence organization,
 and/or
 determining one or more sites of target application.

27. A method of determining, by computer, the response of a cell in any tissue to changes in the cell's environment and/or genetic composition comprising providing a complete genomic DNA sequence for the organism and determining the effect of changes in connectrons
5 due to application of a given exogenous stimulus to the genome.

4. It should be noted that all of the claims, including the dependent claims, are directed to a tetradic relationship between two specific adjacent RNA single-stranded sequences (called C1 and C2 for control sequence 1 and control sequence 2) interact with two distant double-stranded DNA sequences (called T1 and T2 for target sequence 1 and target sequence 2). Claim 20 recites a method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising detecting, by computer, one or more pairs of non-adjacent DNA sequences to which are bound one RNA molecule comprising of two RNA sequences.

5. I wish to state the following referring to pages 5 and 6

of the Examiner's action and in reference to subparagraphs a) through h):

In subparagraph a), the Examiner first states that in order to practice the claimed invention, one skilled in the art must identify and use a connectron to predict the relation of gene expression. Keeping in mind that the claims under consideration are directed to computer mediated methods of analysis of connectron sequences, I disagree with the Examiner's conclusion that there would be an unpredictable amount of experimentation required to practice the claimed invention.

The skilled practitioner would turn to the instant description and drawings for guidance in using the claimed invention. The specification provides a detailed roadmap for practicing the invention by one skilled in the art. Referring specifically to the specification and drawings, the introduction at pages 1 - 3 provides a basic description of connectron structure. Figures 1 - 3 are taken from the text by Alberts et al. entitled "The Molecular Biology of the Cell." Pages 3 - 25. Pages 26 - 36 provides a detailed description of a connectron structure. Page 31, the detailed description of the invention, provides a descriptive analysis of the flow diagrams utilized in the computer analysis of connectrons in any given genome. Additionally, ten samples of connectrons found by computer mediation are set out in the specification. Pages 39 - 56 give an example of a prokaryote connectron - E. coli. Hence, the algorithm is clearly defined and

could be programmed by a skilled scientist. In this sense, the amount of experimentation is quite predictable.

I agree that the nature of the invention, gene control, is complex, and that prior art does not discuss connectron symmetries; i.e., it is my understanding and belief that the connectron invention disclosed in the instant application was made by the inventor, Richard J. Feldmann.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date:

6/5/03

(Signature)

Name:

Richard W. Paster

June, 2003

CURRICULUM VITAE

Richard W. Pastor, Ph.D.

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Date of Birth: June 21, 1951

Citizenship: United States

Education:

- 1984 Ph.D. Harvard University, Biophysics
Dissertation Title: *Topics in Stochastic Dynamics of Polymers*. Preceptor: Martin Karplus
- 1977 M.S. Syracuse University, Chemistry
Thesis Title: *Surface Tension Calculations for Molten Salts: Critique and Modification of the Kirkwood-Buff Model*.
Preceptor: Jerry Goodisman
- 1973 B.A. Hamilton College, Major in Philosophy

Employment:

- 1996-Present Chief, Biophysics Laboratory, CBER/FDA
- 1998 Acting Chief, Laboratory of Immunobiochemistry, CBER/FDA
- 1990-1996 Research Chemist, Biophysics Lab, CBER/FDA
- 1984-1990 Senior Staff Fellow, Biophysics Lab, CBER/FDA
- 1984 Staff Fellow, Laboratory of Chemical Physics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

Awards:

- 1997 *Center Director's Public Health Achievement Award*
Center for Biologics Evaluation and Research
- 1996 *Scientific Achievement - Senior Investigator*
Center for Biologics Evaluation and Research
- 1996 *Excellence in Science by a Group*
Food and Drug Administration
- 1977 *Teaching Assistant of the Year*
Department of Chemistry, Syracuse University

Research Area: The application of computer simulations and statistical mechanics to biophysics, with emphasis on membranes.

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Teaching:

- 1994 Adjunct Professor, George Mason University
Physical Biochemistry
- 1978-1980 Teaching Fellow, Harvard University
Physical Biochemistry and Introductory Biochemistry
- 1975-1977 Teaching Fellow, Syracuse University
General Freshman and Honors Freshman Chemistry

Publications

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FDA Guidance Documents:

Testing Limits in Stability Protocols for Standardized Grass Pollen Extracts

Potency Limits for Standardized Dust Mite and Grass Allergen Vaccines: A Revised Protocol